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EXAMINER	
HAMA, JOANNE	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/500,240	WILDT ET AL.	
	Examiner	Art Unit	
	Joanne Hama, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 March 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-12 and 14-65* is/are pending in the application.

4a) Of the above claim(s) *18-45,47-58 and 60-65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-12,14-17,46 and 59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Election/Restrictions

Applicant's election of Group 1a in the reply filed on March 27, 2007 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). It is noted that Applicant also provided a species election for the value of "X" of $GlcNAcMan_XGlcNAc_2$. Applicant indicates "X" is 3. It is noted that upon review of the case, that enzymatic processing of $GlcNacMan_5GlcNAc_2$ will yield $GlcNAcMan_3GlcNAc_2$. Because the search for $GlcNAcMan_3GlcNAc$ will also encompass $GlcNacMan_5GlcNAc_2$, the species election as it applies to this election is withdrawn.

It is noted that in addition to the above election, species elections were indicated in Applicant's response on November 11, 2006.

With regard to distinctly named glycosidase and glycotransferases (claim 7), Applicant elected alpha-1, 2, mannosidase. While Applicant did not specifically elect an invention comprising either or glycosidase or glycosyltransferase, as indicated on page 6 of the Restriction, June 29, 2006, it is inferred from this species election that "glycosidase" was elected.

With regard to distinctly named diminished or depleted enzymes (claims 8 and 9), Applicant elected dolichyl-P-Man: Man5GlcNAc2-PP-dolichyl alpha-1,3, mannosyltransferase. It is noted that the yeast homolog of this enzyme is Alg3 (see Korner et al., 1999, The EMBO Journal, 18: 23: 6816-6822, abstract).

With regard to distinctly named sugars (claims 12-15), Applicant elected GlcNac.

With regard to distinctly named host cells (claim 17) Applicant elected Pichia pastoris.

Claims 18-45, 47-58, 60-65 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected Inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on March 27, 2007.

Claims 1-4, 6-12, 14-17, 46, 59 are under consideration.

It is noted that Applicant indicates that the alpha-1,6-mannlsyltransferase (Och1) activity adds mannose to the 1,3 arm of the oligosaccharide structure, not the 1,6 arm of the oligosaccharide structure. Further, the alpha-1,6-mannosyltransferase does not transfer mannose residues to mannose residues on the 1,3 arm of the lipid-linked oligosaccharide structure but adds the mannose residue to the mannose residues on the 1,3 arm of the oligosaccharide structure after the oligosaccharide structure has been transferred to the asparagine residue of a glycoprotein and the glycoprotein has entered the Golgi (Applicant's response, page 10, 4th parag. under "Remarks/Arguments"). In response, during the search of the claimed invention and reading of the specification, the Examiner found that Och1 is an initiation specific enzyme that initiates outer chain mannosylation (on the alpha-1,3 arm of the Man3 core structure) (specification, page 34, lines 4-5, see also Nakanishi-Shindo et al., 1993, The Journal of Biological Chemistry, 268: 26338-26345, abstract). As such, while Och1 yeast mutants are not readable on the claims, it is noted that other yeast comprising mutations in genes

encoding enzymes that add a sugar residue to the 1,6 arm of a lipid-linked oligosaccharide structure were known in the art. This includes the alg3 mutant (Verostek et al., 1991, The Journal of Biological Chemistry, 266: 5547-5551).

Information Disclosure Statement

Applicant filed Information Disclosure Statements (IDSes) on November 8, 2005 and August 22, 2006.

The information disclosure statement filed November 8, 2005 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each cited foreign patent document; each non-patent literature publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. It has been placed in the application file, but the information referred to therein has not been considered. It is noted that reference CM2, Segawa et al., 1999 (IDS filed November 8, 2005), is missing and has not been considered. As such, the reference has been lined through. Should Applicant wish the Examiner to consider the reference, a copy must be provided.

It is also noted that the listing of references in the specification (pages 69-71) is not a proper information disclosure statement. 37 CFR 1.98(b) requires a list of all patents, publications, or other information submitted for consideration by the Office, and MPEP § 609.04(a) states, "the list may not be incorporated into the specification but must be submitted in a separate paper." Therefore, unless the references have been cited by the examiner on form PTO-892, they have not been considered. Should

Applicant wish to have the references cited in the specification to be considered, they must be listed on an IDS and copies of the references must be provided.

Specification

The nucleotide sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

Appropriate correction is required.

While the computer readable format (CRF), paper copy of the sequence, and a letter indicating the listing on the CRF and paper copy are the same have been received (June 25, 2004), the specification, as filed is missing SEQ ID NOs. assigned to the sequences listed in the figures and throughout the specification (e.g. see Figures 4 and 5 and page 53, parag. 173). Each sequence must be assigned a SEQ ID NO.

The absence of proper sequence listing did not preclude the examination on the merits however, **for a complete response to this office action, applicant must submit the required material for sequence compliance.**

Claim Objection

Claims 6 and 46 are objected to for including non-elected subject matter. Note that "glycosyltransferase" has been restricted in claim 6, see above, and that in claim 46, claim 44 is not being examined.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-4, 6, 7, 10, 11, 14-17 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 8-12 of U.S. Patent No. 7,029,872 ('872). Although the conflicting claims are not identical, they are not patentably distinct from each other because both inventions are similarly drawn to methods of making recombinant glycoprotein comprising an N-glycan structure in a

eukaryotic host cell, wherein the method comprises diminishing or depleting one or more enzymes that transfer a sugar residue to the 1,6 arm of a lipid-linked oligosaccharide structure and introducing nucleic acid constructs that express glycosidase. The claims of '872 are a species of the instant claims ('240). The "lower eukaryotic host cell" (claim 1) alpha-1,2 mannosidase catalytic domain (claim 1, point a) of '872 are species of the instant claims. It is noted that while claim 1 of '872 indicates that the product that is being made is $Man_5GlcNac_2$ and not $GlcNAcMan_XGlcNac_2$ (wherein X is 3, 4, 5) of claim 1 of '240, an artisan would have arrived at both types of glycoprotein modifications because the method steps are the same. As such, to make $GlcNAcMan_5GlcNac_2$ in claim 3, point c of '872, adding GlcNAc transferase I is an obvious variant to the method of claim '240 as an artisan already arrives at $GlcNAcMan_XGlcNac_2$, without GlcNAc transferase I. With regard to the claims being drawn to the N-glcyan being further modified to comprise sugar, to have an oligosaccharide branch comprising NeuNAc-GalGlcNAc-Man, to grow in a variety of host cells, and to have the host cell comprise a lack in mannosyltransferases, particularly 1,3 mannosyltransferase, the scope of the claims between '872 (claims 8-12) and '240 (claims 14-17) are the same.

While the claims of '872 are not explicit that the alpha-1,6 mannosyltransferase activity is caused by a mutation (claims 10-11 of '240), '872 indicates that yeasts having altered mannosylations are known in the art and are envisioned to be used in the claimed invention ('872, Table 1).

Claims 1-4, 8-11, 14-17, 59 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1, 3, 8,12, 13, 16-18, 28 of copending Application No. 10/371,877 ('877). Although the conflicting claims are not identical, they are not patentably distinct from each other because both methods are similarly drawn to making N-glycan recombinant glycoprotein in a eukaryotic host cell, wherein the host cell exhibits a diminished or depleted activity of 1,6 transferase activity, wherein the host cell comprises a nucleic acid that overexpresses a glycosidase. It is noted that while claim 1 of '877 yields $Man_5GlcNac_2$ and not $GlcNAcMan_XGlcNac_2$, as does claim 1 of the instant claims ('240), it is noted that the method results in both products because the method steps are the same.

The '877 claims (claim 1) are narrower in scope than the instant claims ('240) as it specifically uses the alpha-1,2 mannosidase catalytic domain be used, As for the method being drawn to making the glycoprotein ('877, claim 12; '240 claim 14), wherein the glycoprotein comprises at least one oligosaccharide branch comprising NeuNAc-Gal-GlcNAc-Man ('877, claim 13; '240 claim 15), and the use of P. pastoris ('877 claim 16; '240 claim 17), the scope between the inventions is the same.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim 46 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-15,18-20 of copending

Application No. 11/187,066 ('066). Although the conflicting claims are not identical, they are not patentably distinct from each other because both inventions are drawn to glycoproteins comprising at least one N-glycan, wherein the N-glycan is $GlcNAcMan_5GlcNAc_2$. The glycoproteins of '066 are smaller in scope than that of the instant invention ('240) as the instant invention is generally drawn to any protein, while the glycoproteins of '066 are drawn to immunoglobulins. It is noted that while '240's claim is broad, the specification indicates that immunoglobulins were envisioned, see Example 6.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-4, 6-12, 14-17, 46, 59 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for

1) a method of producing a recombinant glycoprotein having N-glycans comprising $GlcNAcMan_XGlcNac_2$ core structure (wherein X is 5), wherein the method comprises disrupting Och1 and alg3 in P. pastoris and comprises introducing transgene constructs: 1) a transgene construct comprising 988-1296 nucleotides of yeast SEC12 operably linked to an N-terminal deletion of mouse alpha-1,2-mannosidase IA gene and

2) a transgene construct comprising the first 120 bp of S. cerevisiae MNN9 gene operably linked to human GnTI, which was missing the first 154 bp and

2) a glycoprotein comprising $GlcNAcMan_XGlcNac_2$ (wherein X is 3, 4, 5),

does not reasonably provide enablement for

1) a method of producing a recombinant glycoprotein having N-glycans comprising $GlcNAcMan_XGlcNac_2$ core structure, wherein X is 3, 4, 5 wherein the method comprises disrupting one or more enzymes that transfers a sugar residue to the 1,6 arm of a lipid-linked oligosaccharide structure in any host cell and expressing any glycosidase activity and

2) a method of producing a recombinant glycoprotein having N-glycans comprising $GlcNAcMan_XGlcNac_2$ core structure (wherein X is 3 or 4), wherein the method comprises disrupting Och1 and alg3 in P. pastoris and comprises introducing transgene constructs: 1) a transgene construct comprising 988-1296 nucleotides of yeast SEC12 operably linked to an N-terminal deletion of mouse alpha-1,2-mannosidase IA gene and 2) a transgene construct comprising the first 120 bp of S. cerevisiae MNN9 gene operably linked to human GnTI, which was missing the first 154 bp.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Enablement is considered in view of the Wands factors (MPEP 2164.01(a)). The court in Wands states: "Enablement is not precluded by the necessity for some

experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case are discussed below.

With regard to the scope of non-human eukaryotic host cell and the scope of enzymes used to make $GlcNacMan_XGlcNAc_2$ (wherein X is 5), the specification teaches that P. pastoris was used and that P. pastoris comprised 1) a transgene construct comprising 988-1296 nucleotides of yeast SEC12 operably linked to an N-terminal deletion of mouse alpha-1,2-mannosidase IA gene and 2) a transgene construct comprising the first 120 bp of S. cerevisiae MNN9 gene operably linked to human GnTI, which was missing the first 154 bp (specification, Example 2). However, the specification does not provide guidance for the full breadth of non-human eukaryotic cells and various enzymes, as claimed. According to post-filing art, there were attempts

to re-engineer glycosylation pathways by expressing various enzymes that are involved in early N-glycan processing in humans. However, these attempts failed to eliminate the competing endogenous glycosylation pathways or chose hosts that did not provide an appropriate substrate. For example, work by Harry Schacter and co-workers showed that while active GlcNAcT I could be expressed in A. nidulans, the proteins produced by the engineered strain showed no transfer of GlcNAc to N-glycans. Explanations to describe the result include improper localization of GlcNAcT I, the absence of a $Man_5GlcNac_2$ acceptor substrate at the site of GlcNacT I localization, conditions at the site of localization that were not conducive to GlcNAcT1 activity (e.g. incorrect pH), and lack of UDP-GlcNAc at the site of GlcNAcT I localization. In another situation taught by Conreras and colleagues, expression of alpha 1,2-mannosidase from T. reesei in the secretory pathway of P. pastoris resulted in the production of higher molecular mass glycanse, which is in contrast to the smaller molecular mass glycans one would expect if the enzyme is active in the secretory pathway. These studies highlight the importance of ensuring the absence of competing endogenous reactions and ensuring that an appropriate substrate is available for the corresponding glycosylation enzyme (Wildt and Gerngross, 2005, Nature Review: Microbiology, 3: 119-128; page 123, 1st col., 2nd parag.). As these teachings apply to the instant invention, while the specification teaches one specific combination of host cell, enzymes, and organism from which the enzymes was obtained, the specification does not provide guidance for an artisan to use full breadth of non-human eukaryotic host cells (which include yeasts and non-human mammals), enzymes involved in N-glycosylation, and

organism sources of the enzymes. As such, the claims are limited to P. pastoris was used and that P. pastoris comprised 1) a transgene construct comprising 988-1296 nucleotides of yeast SEC12 operably linked to an N-terminal deletion of mouse alpha-1,2-mannosidase IA gene and 2) a transgene construct comprising the first 120 bp of S. cerevisiae MNN9 gene operably linked to human GnTI, which was missing the first 154 bp.

It is noted that with regard to the enablement of using GnTII, the specification teaches that a library of GnTII constructs were generated (specification, page 57, parag. 183). The specification also teaches that $GlcNAc_2Man_3GlcNac_2$ was produced in a P.pastoris alg3 delection mutant treated with alpha-1,2 mannosidase and GnTII, wherein $GlcNAcMan_3GlcNAc_2$ is converted to $GlcNAc_2Man_3GlcNac_2$ (specification, legend of Figure 21). However, the specification does not teach what GnTII construct in the library could be used to generate $GlcNAc_2Man_3GlcNAc_2$ (claim 6). As taught by Wildt and Gerngross, an artisan cannot reasonably predict from what organism the enzyme should be obtained such that an artisan could carry out the claimed invention. Further, Wildt and Gerngross also teach that there is difficulty in predicting where substrates are processed in the Golgi or ER that an artisan cannot reasonably predict the combination of GnTII, from a particular species of organism, and Golgi targeting signal such that the claimed invention could be practiced to arrive at $GlcNAc_2Man_3GlcNAc_2$.

Similarly, with regard to the claims being drawn to making a glycoprotein that comprise an oligosaccharide branch comprising the structure NeuNac-Gal-GlcNac-Man

(claim 15), Wildt and Gerngross, 2005, teach that making glycoproteins comprising sialic acid (NeuNAc) is not routine in the art. Like the other enzymes that are used in the claimed invention that glycosylate proteins, the enzyme used to sialate sugars would need to be targeted to appropriate site in the Golgi and the substrates for the reaction would need to be at the appropriate site in the Golgi (Wildt and Gerngross, page 127, 1st col. under "Sialic acid transfer-the final step"). Because the specification and art do not provide guidance in selecting the enzyme that sialates sugars, the site at which the reaction occurs and that the substrates in the reaction are localized with the enzyme, an artisan cannot reasonably predict what elements would be required such that the claimed invention could be practiced.

With regard to the scope of diminishing or depleting the activity of one or more enzymes in the host cell, post-filing art indicates that an artisan cannot predict which enzyme or which combination of enzymes that transfers a sugar residue to the 1,6 arm of a lipid-linked oligosaccharide structure can and/or should be deleted, in order to practice the claimed invention. According to Wildt and Gerngross, 2005, the extent to which an alg3, och1 double mutant would be viable and whether the alg3 deletion is sufficiently tight to prevent subsequent addition of alpha-1,6-mannose by alg12p and whether occupancy could be adversely impacted were not known (Wildt and Gerngross, page 126, 1st col., 2nd parag.). As this teaching applies to the claimed invention, while the specification teach a P. pastoris comprising a disruption in alg3/och1, the claims are drawn to one or more enzymes that are diminished or depleted. It is unclear, without guidance, what other singly targeted enzymes are sufficient to prevent subsequent

addition of sugars by other enzymes that transfer or glycosylate sugars to the 1,6 arm of a lipid-linked oligosaccharide structure. It is also unclear which or what combinations of enzymes can be targeted and is not lethal to the host cell. Thus, while there is guidance to practice using P. pastoris comprising a disruption in alg3/och1, there is no guidance for other mutations in enzymes that transfer sugar residues to the 1,6 arm of a lipid-linked oligosaccharide.

Thus, the claims are rejected.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 4 further limits the invention to producing an N-glycan. However, according to claim 1 (upon which claim 4 depends), the only glycan made is N-glycan. It is unclear how claim 4 further limits the claims.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-4, 6, 7, 10,11, 14-17, 46 are rejected under 35 U.S.C. 102(e) as being anticipated by Gerngross, U.S. Patent 7,029,872, patented April 18, 2006.

The applied reference has a common inventor with the instant application. Based upon the earlier effective U.S. filing date of the reference, it constitutes prior art under 35 U.S.C. 102(e). This rejection under 35 U.S.C. 102(e) might be overcome either by a showing under 37 CFR 1.132 that any invention disclosed but not claimed in the reference was derived from the inventor of this application and is thus not the invention "by another," or by an appropriate showing under 37 CFR 1.131.

As described above in the Double Patenting rejection, Gerngross describes a method of making recombinant glycoprotein comprising an N-glycan structure in a eukaryotic host cell, wherein the method comprises diminishing or depleting one or more enzymes that transfer a sugar residue to the 1,6 arm of a lipid-linked oligosaccharide structure and introducing nucleic acid constructs that express glycosidase. It is noted that while claim 1 of Gerngross indicates that the product that is being made is $Man_5GlcNac_2$ and not $GlcNAcMan_XGlcNac_2$ (wherein X is 3, 4, 5) of claim 1 of the instant application, an artisan would have arrived at both types of glycoprotein modifications because the method steps are the same. As such, the interferon produced in Example 1 of Grengross would have the $GlcNAcMan_XGlcNac_2$ glycan. With regard to the claims being drawn to the N-glcyan being further modified to comprise

sugar, to have an oligosaccharide branch comprising NeuNAc-GalGlcNAc-Man, to grow in a variety of host cells, and to have the host cell comprise a lack in mannosyltransferases, particularly 1,3 mannosyltransferase, the scope of the claims between '872 (claims 8-12) and '240 (claims 8, 9, 14-17, 59) are the same. While the claims of '872 are not explicit that the alpha-1,6 mannosyltransferase activity is caused by a mutation (claims 10-11 of '240), '872 indicates that yeasts having altered mannosylations are known in the art and are envisioned to be used in the claimed invention ('872, Table 1).

Thus, Gerngross anticipate the claimed invention.

Claims 1, 4, 10-12, 15-17, 46 are rejected under 35 U.S.C. 102(b) as being anticipated by Chiba et al., 1998, The Journal of Biological Chemistry, 273: 26298-26304, see IDS.

It is noted that claim 1, as written, can be broadly interpreted as a method of making recombinant glycoprotein in a non-human eukaryotic host cell, wherein the only requirement of the method is that one or more enzymes that transfers a sugar residue to the 1,6 arm of a lipid-linked oligosaccharide structure is diminished or depleted. After carrying out that one step, an artisan could expect to arrive at $GlcNAcMan_XGlcNac_2$ (wherein X is 3, 4, 5) and the various other sugar structures described in claims 12, 14 and 15. Note also with regard to the cell expressing a glycosidase activity, the claim can be read that the expression is an endogenous expression.

Chiba et al. teach that CPY was used as a reporter glycoprotein to assess the glycosylation pattern of a triple mutant strain of yeast, wherein the yeast was a mutant for Och1, Mnn1, and Mnn4 (Chiba et al., page 26302, 1st col. under "Oligosaccharide Structures of the Recombinant Triple Mutant Yeast"). As Chiba et al. meet all the steps of the claim 1, claim 1 is anticipated.

Thus, claims 1, 4, 10-12, 15-17, 46 are anticipated.

Claim 46 is rejected under 35 U.S.C. 102(b) as being anticipated by Bischoff and Kornfeld, 1983, The Journal of Biological Chemistry, 258: 7907-7910.

Claim 46 is drawn to the glycoprotein made by the method of claim 1.

Bischoff and Kornfeld teach that a peptide comprising $GlcNAcMan_5GlcNac_2$ was used in an assay to measure alpha-mannosidase activity (Bischoff and Kornfeld, page 7908, 1st col. under "Enzyme Assays").

It is noted that while Bischoff and Kornfeld do not teach the method, as described in claim 1, the product, a glycoprotein comprising an N-glycan was taught by Bischoff and Kornfeld. Absent evidence to the contrary, the glycopeptide taught by Bischoff and Kornfeld is structurally the same as that claimed by the Applicant. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, or "prima facie

obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Thus, Bischoff and Kornfeld anticipate claim 46.

Claim 46 is rejected under 35 U.S.C. 102(b) as being anticipated by Wagner et al., 1996, Glycobiology, 6: 165-175.

Claim 46 is drawn to the glycoprotein made by the method of claim 1.

Wagner et al. teach hemagglutinin (HA) comprising $GlcNAcMan_3GlcNac_2$ following expression in Sf9 cells (Wagner et al., abstract).

It is noted that while Wagner et al. do not teach the method, as described in claim 1, the product, a glycoprotein comprising an N-glycan was taught by Wagner et al. Absent evidence to the contrary, the glycopeptide taught by Wagner et al. is structurally the same as that claimed by the Applicant. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, or "prima facie obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its

fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Thus, Wagner et al. anticipate claim 46.

Claim 46 is rejected under 35 U.S.C. 102(b) as being anticipated by Velasco et al., 1993, The Journal of Cell Biology, 122: 39-51.

Claim 46 is drawn to the glycoprotein made by the method of claim 1.

Velasco et al. teach that ManII modifies the $GlcNAcMan_5GlcNAc_2$ intermediate to complete the mannose trimming reactions and gives rise to $GlcNacMan_3GlcNAc_2$ (Velasco et al., page 40, 1st col. 1st parag.).

It is noted that while Velasco et al. do not teach the method, as described in claim 1, the product, a glycoprotein comprising an N-glycan was taught by Velasco et al. Absent evidence to the contrary, the glycopeptide taught by Velasco et al. is structurally the same as that claimed by the Applicant. Note also that Velasco et al. teach that $GlcNAcMan_5GlcNAc_2$ is processed into $GlcNacMan_3GlcNAc_2$, and it is implied that $GlcNacMan_4GlcNAc_2$ is an intermediate product of the reaction. Where, as here, the claimed and prior art products are identical or substantially identical, or are produced by identical or substantially identical processes, the PTO can require an applicant to prove that the prior art products do not necessarily or inherently possess the characteristics of his claimed product. See In re Ludtke 441 F.2d 660, 169 USPQ 563 (CCPA 1971). Whether the rejection is based on "inherency" under 35 USC 102, or "prima facie

obviousness" under 35 USC 103, jointly or alternatively, the burden of proof is the same, and its fairness is evidenced by the PTO's inability to manufacture products or to obtain and compare prior art products. In re Best, Bolton, and Shaw, 195 USPQ 430, 433 (CCPA 1977) citing In re Brown, 59 CCPA 1036, 459 F.2d 531, 173 USPQ 685 (1972).

Thus, Velasco et al. anticipate claim 46.

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joanne Hama, Ph.D. whose telephone number is 571-272-2911. The examiner can normally be reached Monday through Thursday and alternate Fridays from 9:00-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

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10/500,240

Application No.:

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

- [X] 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).
- [ ] 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).
- [ ] 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).
- [ ] 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."
- [ ] 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).
- [ ] 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).
- [ ] 7. Other: _____

Applicant Must Provide:

- [X] An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".
- [X] An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.
- [X] A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

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